REMARKS

Claims 1 and 3-8 are pending in the instant application. Claims 1 and 3-8 have been rejected. Claim 1 has been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Withdrawn Claim Rejections

Applicants acknowledge the withdrawal of the rejection of claims 1 and 3-8 under 103(a) as being obvious over Wasner et al., Hannoush et al. and Denisov.

II. Rejection of Claims Under 35 U.S.C. §103

Claims 1 and 3-8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hannoush et al. (Document AE, PTO-1449 filed 10/4/04) in view of Denisov et al. ((2001) *Nucl. Acids Res.* 29:4284-4293). The Examiner suggests that Hannoush et al. teach a hairpin loop structure comprising a tetranucleotide loop having SEQ ID NO:1 having increased duplex stability. The Examiner acknowledges that Hannoush et al. do not teach that this molecule inhibits RNase H activity, but that this molecule is a useful structural motif for synthetic ribozymes and nucleic acid aptamers. It is suggested that Hannoush et al. further teach the hairpin in nucleic acids comprising a tetraloop and a 2′,5′ linkage can form superstable hairpin structures of comparable thermodynamic stabilities and this hairpin formation may be important in the design of novel nucleic acid enzymes as well as antisense agents. The Examiner concludes that because Hannoush et al. teach a stable hairpin structure that is an important

structural motif of use in the design of ribozyme as well as antisense agents, one of skill in the art would have been motivated to incorporate a ANA into the hairpin structure, as taught by Denisov et al. for increased duplex stability. The Examiner concludes that Hannoush et al. in view of Denisov et al. were relied upon to teach a stable hairpin structure useful as an antisense agent and incorporation of ANA would further increase the duplex stability and target specificity.

Claims 1 and 3-8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wasner et al. in view of Hannoush et al. and in further view of Ray et al. ((2000) *FASEB J.* 14:1041-1060). The Examiner suggests that Ray et al. was relied upon to teach incorporation of a PNA into a duplex to increase stability and specificity and further because PNAs have very specific interactions with RNA or DNA making them very promising in therapeutic applications. It is suggested that Ray et al. teach that there are 3 to 4 major applications for PNAs, one of which is that PNAs have a strong affinity for DNA and can be used to bind to DNA and inhibit antigene activity. Further, it is suggested that Ray et al. teach that PNAs, despite their remarkable nucleic acid binding ability, are in general not capable of eliciting RNase activity and further a PNA/RNA chimera that can activate RNase activity is very sequence specific wherein certain sequences have RNase activity while other do not. The Examiner suggests that because the claims are broadly drawn to inhibition of RNase activity of the reverse transcriptase, one of skill in the art would be motivated to incorporate a PNA into a duplex taught by Wasner et al. to increase the duplex stability and specificity to a DNA to decrease antigene activity.

Applicants respectfully disagree with these rejections.

At the outset, Applicants respectfully wish to point out that the instant inhibitory agent is NOT an antisense molecule or a synthetic ribozyme. The inhibitory agent of the present invention is a nucleic acid-based ligand which binds directly to, and inhibits the activity of, the RNase H domain of retroid virus reverse transcriptase. See paragraph [0063] of the published application. Accordingly, to clarify the activity of the instant inhibitory agent, claim 1 has been amended, as supported by the disclosure at paragraph [0063], to indicate that the inhibitory agent binds to the RNase H domain of retroid virus reverse transcriptase thereby inhibiting the RNase H activity thereof.

In this regard, the instant inhibitory agent is an antagonist ligand which has sequence and structural characteristics specific for binding to the substrate pocket of the RNase H domain of reverse transcriptase. Therefore, Applicants respectfully disagree with the Examiner's lines of reasoning that "because Hannoush et al. teach a stable hairpin structure that is an important structural motif [of] use in the design of ribozyme as well as antisense agents, one of skill in the art would have been motivated to incorporate a ANA into the hairpin structure, as taught by Denisov et al. for increased duplex stability" and "[b]ecause the instant claims are broadly drawn to inhibition of RNase activity of the reverse transcriptase, one of skill in the art would be motivated to incorporate a PNA [of Ray et al.] into a duplex taught by Wasner et al. to increase the duplex stability and specificity to a DNA to decrease antigene activity." The mechanism of action of ribozymes and antisense agents is quite different from that of

the instant inhibitory ligand in that ribozymes and antisense agents bind to nucleic acids and the instant inhibitory ligand binds to an enzyme. As such, there would have been no reasonable expectation of success in producing the instant inhibitory agent which binds to and inhibits the RNase H domain of retroid virus reverse transcriptase given the teachings of Hannoush et al pertaining to use of the stable hairpin structure in the design of ribozyme as well as antisense agents, the teachings of Wasner et al. pertaining to duplexes structures lacking hairpins, the teachings of Denisov et al. pertaining to the advantages of using arabinonucleic acid in antisense oligonucleotide analogs, and the teachings of Ray et al. pertaining to the strong DNA affinity of PNAs for use in antisense molecules.

As there is no suggestion or motivation to combine the teachings of Denisov et al. or Ray et al. with that of Wasner et al. and/or Hannoush et al. to produce, with a reasonable expectation of success, an inhibitory agent which binds to the RNase H domain of retroid virus reverse transcriptase thereby inhibiting the RNase H activity thereof, these references fail to make the instant invention obvious in accord with MPEP 2142. It is therefore respectfully requested that these rejections be reconsidered and withdrawn.

III. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record.

Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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